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LETTERS TO THE EDITOR

Bleeding Complications and rt-PA

Both the title and abstract of the report on the Thrombolysis in Myocardial Infarction (TIMI) trial (Mueller et al. [1]) deflect the reader from its central compelling message: 40% of those treated with recombinant tissue-type plasminogen activator (rt-PA) had significant hemorrhage and 22% required blood transfusions.

Although the authors, in their conclusion, discuss the risk of bleeding, the title of their article does not mention this, and the abstract merely says "the frequency of bleeding complications was similar in the four study groups." Nowhere else in the abstract is there any mention of how often bleeding occurred. In my view, these are serious omissions that do a disservice to the practicing cardiologist. Unfortunately, some less than meticulous readers will assume that hemorrhage is not a major problem in this group, particularly if the body of the paper is only skimmed.

We need to know both the risks and the benefits of interventional therapy in acute infarction. The speculation of Mueller et al. may be true: that many of these bleeding events are related to vascular intrusion. This seems reasonable but needs testing. Until that happens, I cannot, in good conscience, recommend rt-PA to my patients knowing that the only data available indicate a hemorrhage rate of 40% and a need for blood transfusion in 22% (with its consequent 5 to 10% risk of hepatitis), particularly when the advantages of reperfusion are equivocal, at best, in patients with inferior infarction.

The pressures to gloss over unwelcome data must be enormous; our journals and their editorial staffs bear a heavy responsibility in making sure this doesn't happen.

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Reply

We agree that report of bleeding complications is important. The main purpose of the article was the comparison of two forms of recombinant tissue-type plasminogen activator (rt-PA) in terms of potency of coronary recanalization. After the initial encouraging results with rt-PA on which the Thrombolysis in Myocardial Infarction (TIMI) investigators reported (1,2), Genentech changed the preparation from a liquid excipient to a lyophilized form. Because the production method of rt-PA differed in important aspects, further testing was essential before the initiation of the large TIMI II trial. Our paper contains two large tables on bleeding complications, which are easily apparent. Further, since the beginning of the TIMI study, several published articles (1–5) have described bleeding complications. They all indicated that hemorrhagic events occurred in >30% of patients, and that 70% of events were observed at catheterization or other vascular puncture sites. They also reported that the frequency of bleeding complications was comparable whether rt-PA or streptokinase was administered (1–3, 5). A report (6) dealing solely with hemorrhagic events and changes in proteins of the fibrinolytic system after rt-PA or streptokinase infusion was recently published. The results of the Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) study (7), also combining rt-PA and coronary angioplasty, were similar to those of our study. Bleeding complications occurred in 38% of patients with the majority of events at vascular puncture sites.

It appears that hemorrhagic events are frequent when thrombolysis is combined with invasive procedures. The currently ongoing TIMI II trial, including infusion of rt-PA alone and in combination with immediate or deferred angioplasty, will provide important information about the impact of procedures on bleeding complications.

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Retrograde Left Ventricular Flow During Early Relaxation

Sasson et al. (1) described the Doppler characteristics of retrograde blood flow within the left ventricle during isovolumic relaxation. They analyzed seven groups of patients and some normal subjects and also reviewed left ventricular angiograms in 13 patients. Careful documentation of these data allowed them to interpret the underlying mechanism of this retrograde left ventricular blood flow.

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